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Search Results - Record(s) 1 through 5 of 5 returned.

☐ 1. Document ID: JP 2007022930 A

L4: Entry 1 of 5 File: JPAB Feb 1, 2007

PUB-NO: JP02007022930A
DOCUMENT-IDENTIFIER: JP 2007022930 A
TITLE: AGENT FOR CONVERTING DENDRITIC CELL FUNCTION AND CONVERSION METHOD

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 2. Document ID: WO 2004076651 A2

L4: Entry 2 of 5 File: EPAB Sep 10, 2004

PUB-NO: WO2004076651A2
DOCUMENT-IDENTIFIER: WO 2004076651 A2
TITLE: GENERATION OF DENDRITIC CELLS FROM MONOCYTIC DENDRITIC PRECURSOR CELLS WITH GM-CSF IN THE ABSENCE OF ADDITIONAL CYTOKINES

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 3. Document ID: JP 2007022930 A

L4: Entry 3 of 5 File: DWPI Feb 1, 2007

DERWENT-ACC-NO: 2007-275839
DERWENT-WEEK: 200727

TITLE: Agent for transforming function of Th2 inductive dendritic cell to Th1 inductive dendritic cell, which is useful for treating atopic dermatitis, contains Calmette-Guerin strain of Mycobacterium bovis, as active ingredient

INVENTOR: AMAGAWA, R; FUKUHARA, S ; ISHII, Y ; TANIGUCHI, M

PRIORITY-DATA: 2005JP-0203690 (July 12, 2005)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE
JP 2007022930 A	February 1, 2007	

INT-CL (IPC): A61K 35/66; A61K 35/74; A61K 39/04; A61P 17/00; A61P 37/00; A61P 37/08

ABSTRACTED-PUB-NO: JP2007022930A
BASIC-ABSTRACT:

NOVELTY - Agent for transforming the function of Th2 inductive dendritic cell to Th1 inductive dendritic cell, comprising Calmette-Guerin strain of Mycobacterium bovis, as an active ingredient, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) drug for treating or preventing disease involving thymuses stromata lymphocyte proliferation factor, comprising Calmette-Guerin strain of M.bovis, as an active ingredient;

(2) transforming the function of Th2 inductive dendritic cell to Th1 inductive dendritic cell, comprising fractionating the blood sample derived from the mammal that produces thymuses stromata lymphocyte proliferation factor from keratinocyte, obtaining dendritic cell fraction, incubating the dendritic cell fraction with Calmette-Guerin strain of M.bovis, in vitro, and detecting the function of dendritic cell in the fraction before and after incubation, and detecting the transformation of the function in Th1 inductive dendritic cell dominance, transformed from Th2 inductive dendritic cell dominance;

(3) treating or preventing disease in a mammal producing thymuses stromata lymphocyte proliferation factor from keratinocyte, comprising administering Calmette-Guerin strain of M.bovis to the mammal; and

(4) a commercial package containing the therapeutic drug for treating or preventing atopic dermatitis.

ACTIVITY - Dermatological.

MECHANISM OF ACTION - Transforms dendritic cell function.

The change in T-cell number was done as follows. The stimulation of CD11c+DC and CD4+ naove T cell in presence or absence of Bacillus Calmette-Guerin (BCG) strain was studied. The T-cell was cocultivated with thymuses stromata lymphocyte proliferation factor (TSLP). After cocultivating for six days, the T cells were collected in fetal bovine serum (FBS) containing RPMI 1640 (10%). The recovered cell was resuspended to the culture solution. Then, trypan-blue dye (0.5%) was added. The survival cell number was counted on calculation board. The absolute number of cytokine producing T cell was calculated. The cytokines were stained and measured using FACScan flowcytometer. Results showed an induction of interleukin (IL)-4 producing T cell (3.0x104 cells) by TSLP stimulation. The induction of IL-4 producing T cell decreased to 1.4x104 cells, in presence of BCG. The induction of interferon (IFN)- gamma producing T-cell increased in presence of BCG. The induction IFN- gamma producing T-cell by BCG addition, indicated functional transformation of Th2 inductive dendritic cell (DC) to Th1 inductive DC.

USE - The agent is useful for treating or preventing disease involving thymuses stromata lymphocyte proliferation factor. The disease is atopic dermatitis (both claimed).

☐ 4. Document ID: US 20030134419 A1

L4: Entry 4 of 5 File: DWPI Jul 17, 2003

DERWENT-ACC-NO: 2003-829641
DERWENT-WEEK: 200377

TITLE: Producing a population of dendritic cell precursors, useful for immunizing humans or animal against a disease, comprises culturing a tissue source in a culture medium containing granulocyte macrophage colony-stimulating factor

INVENTOR: INABA, K; SCHULER, G ; STEINMAN, R M

PRIORITY-DATA: 1994US-0261537 (June 17, 1994), 1992US-0861612 (April 1, 1992), 1992US-0981357 (November 25, 1992), 1993US-0040677 (March 31, 1993), 1999US-0451511 (November 30, 1999), 2002US-0287813 (November 5, 2002)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE
US 20030134419 A1	July 17, 2003	

INT-CL (IPC): C12N 5/00; C12N 5/02

ABSTRACTED-PUB-NO: US20030134419A
BASIC-ABSTRACT:

NOVELTY - Producing a population of dendritic cell precursors from proliferating cell cultures comprises culturing the tissue source on a substrate in culture medium comprising granulocyte macrophage colony-stimulating factor (GM-CSF) and another factor which increases the proportion of dendritic cell precursors by inhibiting the proliferation or maturation of non-dendritic cell precursors.

DETAILED DESCRIPTION - Producing a population of dendritic cell precursors from proliferating cell cultures comprises:

(a) providing a tissue source comprising dendritic cell precursors;

(b) culturing the tissue source on a substrate in culture medium comprising GM-CSF and another factor which increases the proportion of dendritic cell precursors by inhibiting the proliferation or maturation of non-dendritic cell precursors to produce proliferating dendritic cell precursors; and

(c) culturing the dendritic cell precursors for a time to allow them to mature into mature dendritic cells.

INDEPENDENT CLAIMS are also included for the following:

(1) a composition comprising a dendritic cell modified antigen where a substance to be modified is exposed to a culture of dendritic cells prepared from the method above, and the substance is modified by the dendritic cells to produce the modified antigen;

(2) a method of immunizing against disease in humans or animal by administering a composition of (1);

(3) a vaccine comprising the composition of (1);

(4) a composition comprising antigen activated dendritic cells prepared from above which are pulsed with an antigen and the dendritic cells process the antigens to produce a modified antigen, which is expressed by dendritic cells;

(5) a method of treating autoimmune disease by administering to the patient a composition of (4), where the antigen to be modified is a self-protein; and

(6) dendritic cell precursors prepared from the method above.

ACTIVITY - Immunosuppressive; Antiinflammatory; Antidiabetic.

MECHANISM OF ACTION - Vaccine.

USE - The method is useful for producing a population of dendritic cell precursors from proliferating cell cultures. Compositions comprising a dendritic cell modified antigen are useful for immunizing humans or animal against a disease. Compositions comprising antigen activated dendritic cells are useful for treating autoimmune disease such as multiple sclerosis, myasthenia gravis, atopic dermatitis, and juvenile diabetes (claimed). Dendritic cells may be used to produce therapeutic or prophylactic immune response in an individual to treat or prevent infection by drug resistant organisms, e.g. BCG mycobacterium causing tuberculosis. Activated dendritic cells or modified antigens may be formulated as vaccines to prevent future infection or to activate the immune system to treat ongoing disease.

☐ 5. Document ID: IN 200400481 P4, WO 2003022215 A2, EP 1441591 A2, AU 2002326846 A1, NO 200400965 A, BR 200212545 A, JP 2005505270 W, US 20050059151 A1, MX 2004002147 A1, CN 1636229 A, KR 2005027163 A, IN 200400480 P4

L4: Entry 5 of 5 File: DWPI Dec 23, 2005

DERWENT-ACC-NO: 2003-313181
DERWENT-WEEK: 200604

TITLE: Producing mature dendritic cells, by contacting immature dendritic cells with Bacille Calmette-Guerin and interferon gamma for maturation of immature cells, so that mature cells produce increased IL-12 to IL-10 ratio

INVENTOR: BOSCH, M L; HAFER, J ; ROSENTHAL, D ; SUDAU, P

PRIORITY-DATA: 2001US-317569P (September 6, 2001), 2004US-0488744 (March 5, 2004)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE
IN 200400481 P4	December 23, 2005	E
WO 2003022215 A2	March 20, 2003	E
EP 1441591 A2	August 4, 2004	E
AU 2002326846 A1	March 24, 2003	
NO 200400965 A	April 23, 2004	
BR 200212545 A	January 18, 2005	
JP 2005505270 W	February 24, 2005	
US 20050059151 A1	March 17, 2005	
MX 2004002147 A1	March 1, 2005	
CN 1636229 A	July 6, 2005	
KR 2005027163 A	March 17, 2005	

IN 200400480 P4 December 23, 2005 E

INT-CL (IPC): A01N 63/00; A61K 0/00; A61K 35/12; A61K 35/14; A61K 45/00; A61P 37/04; B21B 1/26; B21B 1/46; C07K 14/52; C12N 5/00; C12N 5/02; C12N 5/06; C12N 5/08; C12N 15/86; G06K 19/00

ABSTRACTED-PUB-NO: WO2003022215A
BASIC-ABSTRACT:

NOVELTY - Producing (M1) a mature dendritic cell population (I), comprising contacting immature dendritic cells (II) with Bacille Calmette-Guerin (BCG) and interferon gamma (IFN gamma) for maturation of (II), is new. (I) produces an increased ratio of interleukin (IL)-12 to IL-10 than (II) not contacted with BCG and IFN gamma during maturation, or (I) produces a type 1 immune response.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a composition (C) for activating T cells, comprising a dendritic cell population matured with an effective concentration of BCG and IFN gamma under suitable conditions for maturation, and a predetermined antigen, where the dendritic cell population produces an increased ratio of IL-12 to IL-10 than a mature dendritic cell population contacted with BCG without IFN gamma during maturation;

(2) an isolated, immature dendritic cell population, comprising isolated immature monocytic dendritic cells, and an effective concentration of BCG and IFN gamma to induce maturation of the immature dendritic cells, where the resulting mature dendritic cells produce more IL-12 to IL-10;

(3) isolated mature dendritic cells producing more IL-12 to IL-10 prepared by maturation of (II) with a composition comprising effective concentrations of BCG and IFN gamma under conditions suitable for the maturation of (II); and

(4) isolated mature dendritic cells loaded with a predetermined antigen, the dendritic cells producing more IL-12 than IL-10.

ACTIVITY - None given.

MECHANISM OF ACTION - Induces maturation of immature dendritic cells; Produces Type 1 immune response; Activates T cells (claimed).

Dendritic cells (DCs) matured in the presence of BCG and IFN gamma were demonstrated to elicit a significantly higher tumor-specific T cell IFN gamma release and similar levels of antigen-specific cytotoxicity as compared to DCs matured with BCG alone. Immature dendritic cells were isolated and cultured in the presence of granulocyte macrophage-colony stimulating factor (GM-CSF) and IL-4. The DCs were then loaded with either whole tumor cells (A549) previously infected with recombinant adenovirus expressing either green fluorescent protein (GFP) or the M1 protein of influenza A virus. The DCs were matured 24 hours later with either BCG or BCG in combination with IFN gamma . The tumor loaded DCs or GFP or M1-expression tumor cells were used to stimulate an autologous M1-specific T cell line. Twenty-four hours later, cell culture supernatants were harvested and run on a standard IFN gamma enzyme linked immunosorbent assay (ELISA). Only DCs loaded with M1-expression tumor cells were able to stimulate IFN gamma release and DCs matured in BCG plus IFN gamma were significantly more potent at inducing this response than either immature or BCG matured DCs.

USE - M1 is useful for producing mature dendritic cell population. The obtained mature dendritic cells are useful for producing activated T cells, by performing

M1, and contacting the mature dendritic cells with naive T cells to form an activated T cells producing IFN gamma . The activated T cells are useful for producing type 1 immune response in an animal, by administering the activated T cells to the animal. (All claimed.) The mature dendritic cells are useful for activating and for preparing T cells polarized towards production of type 1 cytokines and/or type 1 response.

ADVANTAGE - The mature dendritic cells produced by M1 produces at least 10-fold more IL-12 than IL-10 (claimed).

Terms	Documents
bcg with dendritic	5

8/3,K,AB/6 (Item 2 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci

06721101 Genuine Article#: ARK45 Number of References: 35
Title: CELLULAR MECHANISMS IN INVIVO PRODUCTION OF GAMMA INTERFERON INDUCED BY LIPOPOLYSACCHARIDE IN MICE INFECTED WITH MYCOBACTERIUM-BOVIS BCG
Author(s): WADA M; OKAMURA H; NAGATA K; SHIMOYAMA T; KAWADE Y
Corporate Source: HYOGO COLL MED,DEPT INTRAMURAL RES,1-1,MUKOGAWACHO/NISHINOMIYA/HYOGO 663/JAPAN/; HYOGO COLL MED,DEPT BACTERIOL/NISHINOMIYA/HYOGO663/JAPAN/; KYOTO UNIV,INST VIRUS RES/KYOTO 606//JAPAN/
Journal: JOURNAL OF INTERFERON RESEARCH, 1985, V5, N3, P431-443
Language: ENGLISH Document Type: ARTICLE

...Title: IN INVIVO PRODUCTION OF GAMMA INTERFERON INDUCED BY LIPOPOLYSACCHARIDE IN MICE INFECTED WITH MYCOBACTERIUM-BOVIS BCG
, 1985
...Research Fronts: CYCLOSPORINE ON T-CELL POPULATIONS AND OTHER INVESTIGATIONS OF ITS IMMUNOSUPPRESSIVE ACTIVITIES)
85-1272 001 (ANTIGEN PROCESSING AND PRESENTATION BY MACROPHAGES, DENDRITIC CELLS AND B-CELLS, ACCESSORY CELL HETEROGENEITY AND MECHANISMS OF T-CELL ACTIVATION IN THE...

8/3,K,AB/4 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

00204877 Genuine Article#: CX545 Number of References: 311
Title: CYTOKINES AND ENDOTHELIAL-CELL BIOLOGY
Author(s): POBER JS; COTRAN RS
Corporate Source: BRIGHAM & WOMENS HOSP,DEPT PATHOL/BOSTON//MA/02115;
HARVARD UNIV,SCH MED,DEPT PATHOL/BOSTON//MA/02115
Journal: PHYSIOLOGICAL REVIEWS, 1990, V70, N2, P427-451
Language: ENGLISH Document Type: REVIEW

, 1990
...Research Fronts: IN CHRONICALLY INFLAMED TISSUES)
88-0096 001 (LEPROMATOUS LEPROSY; PHENOLIC GLYCOLIPID-I OF MYCOBACTERIUM-LEPRAE; BCG ANTIGENS; ICRC ANTILEPROSY VACCINE)
88-0106 001 (BASIC FIBROBLAST GROWTH-FACTOR; EXPRESSION IN CULTURED BOVINE VASCULAR SMOOTH-MUSCLE CELLS; HEPARIN-BINDING DOMAINS)
88-0521 001 (DENDRITIC CELLS; FETAL ISLET ALLOTRANSPLANTATION; ETHANOL ELIMINATION RATE INVIVO; TOLERANCE INDUCTION; ALLOGENEIC LYMPHOCYTES; ADULT HOSTS)
88-0556 001 (T-CELL ACTIVATION; MALARIA CIRCUMSPOROZOITE PROTEIN; ANTIGEN PROCESSING; SYNTHETIC PEPTIDE-BASED VACCINE; MHC MOLECULES IN DETERMINANT SELECTION)
88-1024 001 (HLA CLASS-II GENES; MAJOR...

Collaboration between human blood dendritic cells and monocytes in antigen presentation.

Rasanen L; Lehto M; Hyoty H; Leinikki P
Department of Biomedical Sciences, University of Tampere, Finland.

APMIS - acta pathologica, microbiologica, et immunologica Scandinavica (DENMARK) Nov 1989, 97 (11) p981-6, ISSN 0903-4641--Print
Journal Code: 8803400
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

We compared human blood dendritic cells and monocytes for their capacity to produce secreted and membrane interleukin 1 (IL-1), stimulate mixed leukocyte reaction (MLR) and augment microbial antigen-induced T lymphocyte proliferation. Our enriched ***dendritic*** cell and monocyte fractions contained greater than 80% and greater than 93% dendritic cells and monocytes, respectively. Monocytes produced about ten times higher amounts of membrane and secreted IL-1 than dendritic cells, which in turn were more potent in presenting HLA-DR antigens in MLR. Both accessory cell types presented purified protein derivative of tuberculin (PPD) equally well, whereas monocytes were better with fixed Bacillus Calmette Guerin (***BCG***) bacteria. Processing of ***BCG*** was chloroquine-sensitive. Coculture experiments suggested that there was collaboration or synergy between dendritic cells and monocytes in ***antigen*** ***processing*** and presentation.

Myb-transformed hematopoietic cells as a model for monocyte differentiation into ***dendritic*** cells and macrophages.

Banyer J L; Hapel A J

Experimental Haematology Group, John Curtin School of Medical Research, Australian National University, Canberra, ACT.

Journal of leukocyte biology (UNITED STATES) Aug 1999, 66 (2) p217-23, ISSN 0741-5400--Print Journal Code: 8405628

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Immune induction is effected through the interaction of antigen-presenting cells with specific receptors on the surface of thymus-derived lymphocytes. Cells most able to ingest, ***process*** , and present antigen appear to be related to the mononuclear phagocyte/neutrophil series. For example ***dendritic*** cells (DC) can be found in colonies of GM-CSF-responsive bone marrow cells, and under experimental conditions are routinely expanded as a population in vitro from GM-CSF-responsive progenitor cells. To address the question of DC lineage and to determine what genes are involved in lineage commitment, we have generated a series of GM-CSF-responsive cell lines that can be induced to differentiate in a homogeneous manner in vitro. The cloned cell lines are derived from 12-day fetal liver and are transformed with a truncated form of c-myb, which lacks the normal autoregulatory sequences. As far as we know, these myb-transformed hemopoi-etic cells (MTHC) differ from normal only in the unregulated expression of myb, a gene whose expression is obligatory for proliferation of hemopoietic cells. MTHC in the presence of TNF-alpha and IL-4 will differentiate into cells that have many of the properties of macrophages. When the same MTHC lines are exposed to TNF-alpha in combination with IFN-gamma , the cells instead become DC. The differentiated DC are potent presenters of antigen in mixed lymphocyte reactions and of soluble antigen to specific T cell lines. Thus, cells with the properties of both macrophages and DC can be deriv

Stimulatory and inhibitory differentiation of human myeloid ***dendritic*** cells.

Chakraborty A; Li L; Chakraborty N G; Mukherji B

Department of Medicine, University of Connecticut School of Medicine, Farmington, Connecticut 06030-3210, USA.

Clinical immunology (Orlando, Fla.) (UNITED STATES) Feb ***2000*** , 94 (2) p88-98, ISSN 1521-6616--Print Journal Code: 100883537

Contract/Grant No.: CA 61398; CA; NCI; CA 83130; CA; NCI

Publishing Model Print

Document type: Journal Article; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Dendritic cells (DCs) play a critical obligate role in presenting antigens to T cells for activation. In the ***process*** , upon antigen capture, DCs undergo maturation and become more stimulatory. Human myeloid DCs can be generated from various sources, including blood, bone marrow, and CD34(+) stem cells. As such, plastic-adherent monocytes from circulation have served as a ready source for generating myeloid DCs in culture in granulocyte-macrophage colony-stimulating factor (GM-CSF) and interleukin-4 (IL-4) for translational research in active specific immunotherapy, especially in cancer, with the belief that they are essentially stimulatory or "immunogenic." Here we show that in vitro cultures of plastic-adherent circulating monocytes in GM-CSF and IL-4 followed by further maturation in interferon-gamma plus bacterial superantigens (DC maturing agents) can give rise to two diametrically opposite types of DCs-one stimulatory and another inhibitory. The stimulatory DCs express higher amounts of costimulatory molecules, synthesize IL-12, and efficiently stimulate naive allogeneic T cells in mixed lymphocyte reaction (MLR). The inhibitory DCs, in contrast, express lower concentrations of the critical costimulatory molecules, synthesize large amounts of IL-10, and are nonstimulatory in allogeneic primary MLR. Moreover, while the stimulatory DCs further amplify proliferation of T cells in lectin-driven proliferation assays, the inhibitory DCs totally block T cell proliferation in similar assays, in vitro. Most interestingly, neutralization of the endogenously derived IL-10 with anti-IL-10 antibody in DC cultures repolarizes the inhibitory DCs toward stimulatory phenotype. Accordingly, these observations have important implications in translational research involving myeloid DCs. Copyright 2000 Academic Press.

Stimulatory and inhibitory differentiation of human myeloid ***dendritic*** cells.

... ***2000*** ,

Dendritic cells (DCs) play a critical obligate role in presenting antigens to T cells for activation. In the ***process*** , upon antigen capture, DCs undergo maturation and become more stimulatory. Human myeloid DCs can be generated from various sources, including blood...

... cultures of plastic-adherent circulating monocytes in GM-CSF and IL-4 followed by further maturation in interferon-gamma plus bacterial superantigens (DC maturing agents) can give rise to two diametrically opposite types of DCs-one stimulatory and another...

Descriptors: *Dendritic Cells--immunology--IM; Cell Differentiation ; Cells, Cultured; Culture Media; Cytokines--biosynthesis--BI; Dendritic Cells--cytology--CY; Granulocyte-Macrophage Colony-Stimulating Factor--metabolism--ME; Humans; Immunophenotyping; Interleukin-4 --metabolism...

14/3,K,AB/10 (Item 10 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

12504514 PMID: 10449157

Myb-transformed hematopoietic cells as a model for monocyte differentiation into ***dendritic*** cells and macrophages.

Banyer J L; Hapel A J

Experimental Haematology Group, John Curtin School of Medical Research, Australian National University, Canberra, ACT.

Journal of leukocyte biology (UNITED STATES) Aug 1999, 66 (2) p217-23, ISSN 0741-5400--Print Journal Code: 8405628

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

10/488744
60/317592
09/06/01

7/3,K,AB/6 (Item 1 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2007 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 10820438 IFI Acc No: 2005-0059151
IFI Publication Control No: 2005-0059151 IFI Chemical Acc No: 2005-0014149
Document Type: C
COMPOSITIONS AND METHODS FOR PRIMING MONOCYTIC DENDRITIC CELLS AND T CELLS FOR TH-1RESPONSE; GENERATING MATURE DENDRITIC CELL CULTURE VIA EXPOSURE TO MIXTURE CONTAINING BACILLE CALMETTE-GUERIN (BCG), MULTIPLE INTERLEUKINS AND INTERFERON; IMMUNOTHERAPY AND TREATMENT OF VIRAL INFECTION; TISSUE DIRECTED THERAPY
Inventors: Bosch Marnix L (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Probable Assignee (A1): Northwest Biotherapeutics LLC
Attorney, Agent or Firm: TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834, US
Publication (No,Kind,Date), Applic (No,Date):
US 20050059151 A1 20050317 US 2002488744 20020906
Internat. Convention Pub(No,Date),Applic(No,Date):
WO 2002US28620 20020906
Section 371: 20020906
Section 102(e):20020906
Priority Applic(No,Date): US 2002488744 20020906
Provisional Applic(No,Date): US 60-317569 20010906

Abstract: The present invention provides compositions and methods for inducing maturation of immature dendritic cells (DC) and for priming those cells for inducing a type 1 immune response. The present invention also provides dendritic cell populations useful for activating and for preparing T cells polarized towards production of type 1 cytokines and/or a type 1 response. Similarly, activated, polarized T cell populations, and methods of making the same are provided.

COMPOSITIONS AND METHODS FOR PRIMING MONOCYTIC DENDRITIC CELLS AND T CELLS FOR TH-1RESPONSE...

...GENERATING MATURE ***DENDRITIC*** CELL CULTURE VIA EXPOSURE TO MIXTURE CONTAINING BACILLE CALMETTE-GUERIN (BCG), MULTIPLE INTERLEUKINS AND INTERFERON; IMMUNOTHERAPY AND TREATMENT OF VIRAL INFECTION; TISSUE DIRECTED THERAPY

Abstract: The present invention provides compositions and methods for inducing maturation of immature dendritic cells (DC) and for priming those cells for inducing a type 1 immune response. The present invention also provides dendritic cell populations useful for activating and for preparing T cells polarized towards production of type...

Exemplary Claim:
1. A method for producing a mature ***dendritic*** cell population, comprising: providing immature dendritic cells; and contacting the immature dendritic cells with an effective amount of BCG and Interferon gamma (IFN gamma) under culture conditions suitable for maturation of the immature dendritic cells to form a mature dendritic cell population; wherein the mature dendritic cell population produces an increased ratio of Interleukin 12 to Interleukin 10 than an immature dendritic cell population not contacted with BCG and IFN gamma during ***maturation*** .

Non-exemplary Claims:
2. The method of claim 1, further comprising contacting the immature dendritic cells with a predetermined antigen prior to contacting

with ***BCG*** and IFN gamma...

...3. The method of claim 1, further comprising simultaneously contacting the immature dendritic cells with a predetermined antigen, ***BCG*** and IFN gamma...

...5. The method of claim 1, further comprising: isolating monocytic dendritic cell precursors; and culturing the precursors in the presence of a differentiating agent to form the immature dendritic cells...

...7. The method of claim 5, wherein the monocytic ***dendritic*** cell precursors are isolated from a human subject...

...8. The method of claim 1, wherein the mature ***dendritic*** cells produce a ratio of IL-12 to IL-10 of at least about 1...

...9. A method for producing a mature ***dendritic*** cell population, comprising: providing immature dendritic cells; and contacting the immature dendritic cells with an effective amount of BCG and Interferon gamma (IFN gamma) under culture conditions suitable for maturation of the immature dendritic cells to form a mature dendritic cell population; wherein the mature ***dendritic*** cell population produces a type 1 immune response...

...10. The method of claim 9, further comprising contacting the immature dendritic cells with a predetermined antigen prior to contacting with ***BCG*** and IFN gamma...

...11. The method of claim 9, further comprising simultaneously contacting the immature dendritic cells with a predetermined antigen, ***BCG*** and IFN gamma...

...13. The method of claim 9, further comprising: isolating monocytic dendritic cell precursors; and culturing the precursors in the presence of a differentiating agent to form the immature dendritic cells...

```
      ---  -----  -----------
?  s bcg
      S1   38298  BCG
? s (ifn(w)gamma) (5n) (matur? or activat?)
          175533  IFN
          937965  GAMMA
          584691  MATUR?
         2872623  ACTIVAT?
      S2   11857  (IFN(W)GAMMA) (5N) (MATUR? OR ACTIVAT?)
? s s2 and s1
           11857  S2
           38298  S1
      S3     166  S2 AND S1
? rd

>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
      S4      93  RD  (unique items)
? s dendritic
      S5  161970  DENDRITIC
? s s4 and s5
              93  S4
          161970  S5
      S6       6  S4 AND S5
? rd

>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
      S7       6  RD  (unique items)
? t s7/3,k,ab/1-6
```

7/3,K,AB/4 (Item 1 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)

17002007 BIOSIS NO.: 200200595518
Activation of dendritic cells by BCG
AUTHOR: Fricke Ingo (Reprint); Brandau Sven (Reprint); Jocham Dieter; Boehle Andreas
AUTHOR ADDRESS: Immunotherapie, Research Centre Borstel, Borstel, Germany** Germany
JOURNAL: European Urology Supplements 1 (1): p43 January, 2002 2002
MEDIUM: print
CONFERENCE/MEETING: XVIIth Congress of the European Association of Urology Birmingham, England, UK February 23-26, 2002; 20020223
SPONSOR: European Association of Urology
ISSN: 1569-9056
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

Activation of dendritic cells by BCG
2002
DESCRIPTORS:
...ORGANISMS: PARTS ETC: ***dendritic*** cell
CHEMICALS & BIOCHEMICALS: ***BCG*** --...

Generation of optimal monocyte-derived dendritic cells for immunotherapy: Influence of maturation conditions on antigen presentation

AUTHOR: Bosch M L (Reprint); Crosby P (Reprint); Elgamal A-A (Reprint); Howard T (Reprint); Kelley H (Reprint); Lake T (Reprint); Lin D (Reprint) ; Lodge A (Reprint); McEarchern J (Reprint); Monahan S (Reprint); Salgaller M (Reprint); Shankar G (Reprint); Tjoa B (Reprint); Trimble L (Reprint); Turner A (Reprint); Zhou Y (Reprint)
AUTHOR ADDRESS: North-West Biotherapeutics, Inc., Bothell, WA, USA**USA
JOURNAL: Journal of Investigative Dermatology 117 (4): p1008 October, 2001 2001
MEDIUM: print
CONFERENCE/MEETING: 7th International Workshop on Langerhans Cells Stresa, Italy September 07-09, 2001; 20010907
ISSN: 0022-202X
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

Generation of optimal monocyte-derived dendritic cells for immunotherapy: Influence of maturation conditions on antigen presentation
2001
DESCRIPTORS:
...ORGANISMS: ***BCG*** (Mycobacteriaceae)
ORGANISMS: PARTS ETC: ***dendritic*** cell...
CHEMICALS & BIOCHEMICALS: interferon-gam

21/3,K,AB/20 (Item 1 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 04651874
IFI Chemical Acc No: 2007-0019127
Document Type: C
(A1) ANCILLARY COMPOSITION FOR THE PREPARATION OF COMMITTED MATURE DENTRITIC CELLS; CELL DIFFERENTIATION MIXTURE COMPRISING INTERFERONS, MICROSOMES AND RIBOSOMAL COMPONENTS FOR USE IN GENERATION OF ANTIGEN PRESENTING CELLS
(B2) ANCILLARY COMPOSITION FOR THE PREPARATION OF COMMITTED MATURE DENTRITIC CELLS
Inventors: Abastado Jean-Pierre (FR); Boccaccio Claire (FR); Nardin Alessandra (FR)
Assignee: (A1) Unassigned Or Assigned To Individual
(B2) I D M Immuno Designed Molecules FR
Assignee Code: (A1) 68000
Probable Assignee (A1): IDM Immuno-Designed Molecules FR
Attorney, Agent or Firm: Young & Thompson
Publication (No,Kind,Date), Applic (No,Date):
US 20040197901 A1 20041007 US 2001466186 20011229
US 7252996 B2 20070807 US 2001466186 20011229
Calculated Expiration: 20211229
Notes: Subject to any Disclaimer, the term of this patent is extended or adjusted under 35 USC 154(b) by 68 days.
Prior Publication(No,Date),Applic(No,Date):US 20040197901 A1 20041007
Internat. Convention Pub(No,Date),Applic(No,Date): WO 200205567 20020718 WO 2001EP1531 20011229
Section 371: 20031219
Section 102(e):20031219
Priority Applic(No,Date): EP 2001400109 20010115

Abstract: (US 20040197901 A1)
The invention consists in the use of a maturation agent comprising a mixture of ribosomal and/or membrane fractions for the preparation of mature ***dendritic*** cells from immature ***dendritic*** cells.

Abstract: (US 7252996 B2)
The invention consists in the use of a maturation agent comprising a mixture of ribosomal and/or membrane fractions for the preparation of mature ***dendritic*** cells from immature ***dendritic*** cells.

...Internat. Convention Pub(No,Date),Applic(No,Date): ***20020718***

Abstract: ...agent comprising a mixture of ribosomal and/or membrane fractions for the preparation of mature dendritic cells from immature ***dendritic*** cells...

...agent comprising a mixture of ribosomal and/or membrane fractions for the preparation of mature dendritic cells from immature ***dendritic*** cells.

Exemplary Claim:
...comprising a bacterial mixture of ribosomal and/or membrane fractions for the preparation of mature dendritic cells from immature ***dendritic*** cells...

...D R A W I N G

1. A method for the preparation of mature ***dendritic*** cells from immature dendritic cells, comprising treating said immature dendritic cells with a maturation agent comprising a bacterial

mixture of ribosomal fractions or ribosomal and membrane fractions to obtain mature ***dendritic*** cells.

Non-exemplary Claims:

...2. A maturation agent according to claim 1, wherein the maturation agent comprises interferon- gamma and a bacterial mixture of ribosomal and/or membrane fractions...

...3. Process for the preparation of mature ***dendritic*** cells from immature dendritic cells, said process comprising the step of contacting in a culture medium immature dendritic cells with a maturation agent comprising a bacterial mixture of ribosomal and/or membrane fractions...

...4. Process for the preparation of mature ***dendritic*** cells according to claim 3, characterized in that the maturation agent comprises interferon- gamma and a bacterial mixture of ribosomal and/or membrane fractions...

...5. Process for the preparation of mature ***dendritic*** cells according to claim 3, the membrane fractions being from the bacterial strain Klebsiella pneumoniae...

...6. Process for the preparation of mature ***dendritic*** cells according to claim 3, the ribosomal fraction being from the bacterial strains Klebsiella pneumoniae...

...7. Process for the preparation of mature ***dendritic*** cells according to claim 3, said maturation agent comprising a bacterial mixture of ribosomal and...

...8. Process for the preparation of mature ***dendritic*** cells according to claim 3, said maturation agent comprising interferon-y used at a dose ...

...9. ***Dendritic*** cells liable to be obtained according to the process of claim 3...

...10. Pharmaceutical compositions containing as active substance dendritic cells according to claim 9, in association with a pharmaceutically acceptable vehicle...

...11. Cellular vaccine composition containing as active substance ***dendritic*** cells according to claim 9...

...12. Process for the preparation of mature ***dendritic*** cells according to claim 4, the membrane fractions being from the bacterial strain Klebsiella pneumoniae...

...13. Process for the preparation of mature ***dendritic*** cells according to claim 4 the ribosomal fraction being from the bacterial strains Klebsiella pneumoniae...

...14. Process for the preparation of mature ***dendritic*** cells according to claim 5, the ribosomal fraction being from the bacterial strains Klebsiella pneumoniae...

...15. Process for the preparation of mature ***dendritic*** cells according to claim 4, said maturation agent comprising a bacterial mixture of ribosomal and...

...16. Process for the preparation of mature ***dendritic*** cells according to claim 5, said maturation agent comprising a bacterial mixture of ribosomal and...

...17. Process for the preparation of mature ***dendritic*** cells according to claim 6, said maturation agent comprising a bacterial mixture of ribosomal and...

...18. Process for the preparation of mature ***dendritic*** cells according to claim 4, said maturation agent comprising interferon-y

09442413 Genuine Article#: 404RW Number of References: 38
Title: Differential regulation of human blood dendritic cell subsets by IFNs (ABSTRACT AVAILABLE)
Author(s): Ito T (REPRINT) ; Amakawa R; Inaba M; Ikehara S; Inaba K; Fukuhara S
Corporate Source: Kansai Med Univ,Dept Internal Med 1,10-15 Fumizono Cho/Moriguchi/Osaka 5708506/Japan/ (REPRINT); Kansai Med Univ,Dept Internal Med 1,Moriguchi/Osaka 5708506/Japan/; Kansai Med Univ,Dept Pathol 1,Moriguchi/Osaka 5708506/Japan/; Kyoto Univ,Grad Sch Biostudies , Dept Anim Dev & Physiol,Kyoto//Japan/
Journal: JOURNAL OF IMMUNOLOGY, 2001, V166, N5 (MAR 1), P2961-2969
ISSN: 0022-1767 Publication date: 20010301
Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA
Language: English Document Type: ARTICLE
Abstract: Based on the relative expression of CD11c and CD1a, me previously identified subsets of dendritic cells (DCs) or DC precursors in human peripheral blood. A CD1a(+)/CD11c(+) population (CD11c(+) DCs), also called myeloid DCs, is an immediate precursor of Langerhans cells, whereas a CD1a(-)/CD11c(-) population (CD11c(-) DCs), sometimes called lymphoid DCs but better known as plasmacytoid DCs, is composed of type I IFN (IFN-alpha beta)-producing cells. Here, we investigate the effects of IFN-alpha beta and IFN-gamma as well as other cytokines on CD11c(+) and CD11c(-) DC subsets, directly isolated from the peripheral blood, instead of in vitro-generated DCs. IFN-gamma and IFN-alpha, rather than GM-CSF, mere the most potent cytokines for enhancing the maturation of CD11(c)+ DCs, Incubation of CD11c(+) DCs with IFN-gamma also resulted in increased IL-12 production, and this IL-12 allowed DCs to increase Th1 responses by alloreactive T cells. In contrast, IFN-alpha did not induce IL-12 but, rather, augmented IL-10 production. IFN-alpha -primed matured CD11c(+) DCs induced IL-10-producing regulatory T cells; however, this process was independent of the DC-derived IL-10, On the other hand, IFN-alpha by itself neither matured CD11c(-) DCs nor altered the polarization of responding T cells, although this cytokine was a potent survival factor for CD11c(-) DCs. Unlike IFN-alpha, IL-3 was a potent survival factor and induced the maturation of CD11c(-) DCs, The IL-3-primed CD11c(-) DCs activated T cells to produce IL-10, ZFN-gamma, and IL-4. Thus, CD11c(+) and CD11c(-) DC subsets play distinct roles in the cytokine network, especially their responses to IFNs.

21/3,K,AB/9 (Item 2 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)

15548876 BIOSIS NO.: 200000267189
Interferon gamma (IFN-gamma) induces maturation of the dendritic cells which infiltrate into the pyloric mucosa of mongolian gerbil treated with Helicobacter pylori and N-methyl-N'-nitro-N-nitrosoguanidine (MNNG)
AUTHOR: Oka Masashi (Reprint); Ichinose Masao (Reprint); Yahagi Naohisa (Reprint); Shimizu Yasuhito (Reprint); Suzuki Takehisa (Reprint); Matsubara Yasuo (Reprint); Kato-Tsukada Shinko (Reprint); Tateishi-Niihata Ayako (Reprint); Kido Masahiro (Reprint); Tsuji Masahiro (Reprint); Kurakata Shigenori (Reprint); Omata Masao (Reprint)
AUTHOR ADDRESS: Univ of Tokyo, Tokyo, Japan**Japan
JOURNAL: Gastroenterology 118 (4 Suppl. 2 Part 1): pAGA A762 April, 2000
2000
MEDIUM: print
CONFERENCE/MEETING: 101st Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week. San Diego, California, USA May 21-24, 2000; 20000521
SPONSOR: American Gastroenterological Association
ISSN: 0016-5085
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

Interferon gamma (IFN-gamma) induces maturation of the dendritic cells which infiltrate into the pyloric mucosa of mongolian gerbil treated with Helicobacter pylori and...
2000
DESCRIPTORS:
ORGANISMS: PARTS ETC: ***dendritic*** cell...
CHEMICALS & BIOCHEMICALS: ... ***dendritic*** cell marker

21/3,K,AB/10 (Item 1 from file: 34)
DIALOG(R)File 34:SCISEARCH(R) CITED REF SCI

10388982 Genuine Article#: 520FU Number of References: 31

518100 PMID: 11752904

Antigen presentation by murine peritoneal cavity macrophage-derived ***dendritic*** cells.

Makala L H; Nishikawa Y; Kamada T; Xuan X; Nagasawa H

National Research Center for Protozoan Diseases, Obihiro University of Agriculture and Veterinary Medicine, Inada-Cho, Obihiro, Hokkaido, Japan.

Pathobiology - journal of immunopathology, molecular and cellular biology (Switzerland) 2001, 69 (2) p104-12, ISSN 1015-2008--Print

Journal Code: 9007504

Publishing Model Print

Document type: Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Murine peritoneal cavity macrophage derived dendritic cells (PEC-DC) generated using early growth factors, interleukin 4 and granulocyte-macrophage colony-stimulating factor followed by maturation in interferon-gamma plus either, Toxoplasma lysate antigen (TLA) or lipopolysaccharide, bind TLA by a nonspecific mechanism and continue to express major histocompatibility complex class II antigens after 24 h of culture in vitro. Moreover, the proliferation of CD3+ spleen T cells from mice immunized with Toxoplasma gondii homogenate, induced by PEC-DC-mediated antigen presentation was statistically significant and of consistent amplitude. This accessory function of PEC-DC is antigen specific. Copyright 2001 S. Karger AG, Basel

Antigen presentation by murine peritoneal cavity macrophage-derived ***dendritic*** cells.

... ***2001*** ,

Murine peritoneal cavity macrophage derived

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? s (immature or (in(w)vitro) (5n)dendritic
>>>Unmatched parentheses
? s (immature or (in(w)vitro)) (5n) dendritic
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Processing
Processing
Processing
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Processing
Processing
Processing
Processing
          159167  IMMATURE
        40008373  IN
         1628660  VITRO
         1623480  IN(W)VITRO
          161925  DENDRITIC
      S1    7423  (IMMATURE OR (IN(W)VITRO)) (5N) DENDRITIC
? s (partial? (2n) mature?) (5n) dendritic
         1445917  PARTIAL?
          324035  MATURE?
          161925  DENDRITIC
      S2       6  (PARTIAL? (2N) MATURE?) (5N) DENDRITIC
? s s1 or s2
            7423  S1
               6  S2
      S3    7426  S1 OR S2
? s inject? or administ?
         1316647  INJECT?
         2694178  ADMINIST?
      S4 3627839  INJECT? OR ADMINIST?
? s s3 and s4
            7426  S3
         3627839  S4
      S5    1101  S3 AND S4
? s cancer? or tumor? or malignan? or neoplas? or immunotherapy
Processing
         1919078  CANCER?
         2264436  TUMOR?
          671777  MALIGNAN?
         2378052  NEOPLAS?
          105451  IMMUNOTHERAPY
      S6 4530193  CANCER? OR TUMOR? OR MALIGNAN? OR NEOPLAS? OR
                  IMMUNOTHERAPY
? s s5 and s6
            1101  S5
         4530193  S6
      S7     534  S5 AND S6
? rd

>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
      S8     372  RD  (unique items)
? s s8 and py<=2002
Processing
Processing
             372  S8
        44832382  PY<=2002
      S9     143  S8 AND PY<=2002
? s (in(w)vitro) (5n) dendritic
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Processing
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40008373 IN
1628660 VITRO
161925 DENDRITIC
S10 4226 (IN(W)VITRO) (5N) DENDRITIC
? s s9 not s10
143 S9
4226 S10
S11 39 S9 NOT S10
? s cd80 or cd86 or cd54
12638 CD80
11980 CD86
6575 CD54
S12 21459 CD80 OR CD86 OR CD54
? s s11 and s12
39 S11
21459 S12
S13 3 S11 AND S12
? t s13/3,k,ab/1-3

13/3,K,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14020155 PMID: 12393401
Stressed apoptotic tumor cells stimulate dendritic cells and induce specific cytotoxic T cells.
Feng Hanping; Zeng Yi; Graner Michael W; Katsanis Emmanuel
Department of Pediatrics, Steele Memorial Children's Research Center, University of Arizona, Tucson 85724, USA.
Blood (United States) Dec 1 2002, 100 (12) p4108-15, ISSN 0006-4971--Print Journal Code: 7603509
Publishing Model Print-Electronic
Document type: Journal Article; Research Support, Non-U.S. Gov't
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
We have previously reported that stressed apoptotic tumor cells are more immunogenic in vivo than nonstressed ones. Using confocal microscopy we have confirmed our previous observation that heat-stressed apoptotic 12B1-D1 leukemia cells (BCR-ABL(+)) express HSP60 and HSP72 on their surface. To explore how the immune system distinguishes stressed from nonstressed apoptotic tumor cells, we analyzed the responses of dendritic cells to these 2 types of apoptotic cells. We found that nonstressed and heat-stressed apoptotic 12B1-D1 cells were taken up by dendritic cells in a comparable fashion. However, when stressed apoptotic 12B1-D1 cells were coincubated with immature dendritic cells for 24 hours, this resulted in greater up-regulation of costimulatory molecules (CD40, CD80, and CD86) on the surface of dendritic cells. Moreover, stressed apoptotic 12B1-D1 cells were more effective in stimulating dendritic cells to secrete interleukin-12 (IL-12) and in enhancing their immunostimulatory functions in mixed leukocyte reactions. Furthermore, we demonstrated that immunization of mice with stressed apoptotic 12B1-D1 cells induced the secretion of T helper-1 (T(H)1) profile of cytokines by spleen cells. Splenocytes from mice immunized with stressed apoptotic cells, but not nonstressed ones, were capable of lysing 12B1-D1

and the parental 12B1 line, but not a B-cell leukemia line, A20. Our data indicate that stressed apoptotic tumor cells are capable of providing the necessary danger signals, likely through increased surface expression of heat shock proteins (HSPs), resulting in activation/maturation of dendritic cells and, ultimately, the generation of potent antitumor T-cell responses.

Stressed apoptotic tumor cells stimulate dendritic cells and induce specific cytotoxic T cells.
... ***2002*** ,
We have previously reported that stressed apoptotic tumor cells are more immunogenic in vivo than nonstressed ones. Using confocal microscopy we have confirmed...

... HSP72 on their surface. To explore how the immune system distinguishes stressed from nonstressed apoptotic tumor cells, we analyzed the responses of dendritic cells to these 2 types of apoptotic cells...

... cells in a comparable fashion. However, when stressed apoptotic 12B1-D1 cells were coincubated with immature dendritic cells for 24 hours, this resulted in greater up-regulation of costimulatory molecules (CD40, ***CD80*** , and ***CD86***) on the surface of dendritic cells. Moreover, stressed apoptotic 12B1-D1 cells were more effective...

... line, but not a B-cell leukemia line, A20. Our data indicate that stressed apoptotic tumor cells are capable of providing the necessary danger signals, likely through increased surface expression of...
; Animals; Bone Marrow Cells; Cancer Vaccines--administration and dosage--AD; Cancer Vaccines--pharmacology--PD; Chaperonin 60 --metabolism--ME; HSP72 Heat-Shock Proteins; Heat-Shock Proteins --metabolism...

...pathology--PA; Lymphocyte Activation--immunology--IM; Lymphocyte Culture Test, Mixed; Mice; Mice, Inbred BALB C; Tumor Cells, Cultured
Chemical Name: Cancer Vaccines; Chaperonin 60; HSP72 Heat-Shock Proteins; Heat-Shock Proteins

13/3,K,AB/2 (Item 1 from file: 34)
DIALOG(R)File 34:SCISEARCH(R) CITED REF SCI

09905708 Genuine Article#: 463AL Number of References: 43
Title: Enhanced maturation and functional capacity of monocyte-derived immature dendritic cells by the synthetic immunomodulator Murabutide (ABSTRACT AVAILABLE)
Author(s): Vidal V; Dewulf J; Bahr GM (REPRINT)
Corporate Source: Inst Pasteur,Lab Mol Immunol Infect & Inflammat,1 Rue Prof Calmette,BP 245/F-59019 Lille//France/ (REPRINT); Inst Pasteur,Lab Mol Immunol Infect & Inflammat,F-59019 Lille//France/; ISTAC Biotechnol,Lille//France/
Journal: IMMUNOLOGY, 2001, V103, N4 (AUG), P479-487
ISSN: 0019-2805 Publication date: 20010800
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND
Language: English Document Type: ARTICLE
Abstract: Murabutide is a safe synthetic immunomodulator derived from muramyl dipeptide, the smallest bioactive unit of bacterial peptidoglycan. Although it is well known that muramyl peptides modulate the functions of monocytes/macrophages, their activity on dendritic cells is poorly documented. We thus investigated the effects of Murabutide on immunophenotype, endocytosis, T-cell stimulatory capacity, and cytokine secretion of human monocyte-derived ***immature*** ***dendritic*** cells (iDCs). We found that Murabutide

triggers immunophenotypic changes as upon treatment, iDCs up-regulate the surface expression of the major histocompatibility complex type II molecule human leucocyte antigen-DR, the co-stimulatory molecules CD80, CD86 and CD40 and the differentiation marker CD83, and down-regulate the expression of the mannose receptor. These phenotypic changes are also mirrored by changes in their biological activity. Subsequent to treatment with the synthetic immunomodulator, DC have a decreased endocytic capacity but exhibit enhanced stimulatory capacity for both allogeneic and autologous T cells. In addition, Murabutide-stimulated iDCs have a greater cytostatic activity toward the tumour cell line THP-1. Furthermore, in the presence of Murabutide, DCs transiently increased the release of macrophage inhibitory protein-1 beta, tumour necrosis factor-alpha and interleukin-10, whereas the enhanced production of macrophage-colony stimulating factor was sustained over the 3-day period analysed. In addition, Murabutide triggers the phosphorylation of the three classes of mitogen-activated protein kinases in iDCs. Altogether our results demonstrate that Murabutide triggers the maturation and activation of monocyte-derived iDCs. As this immunomodulator is approved for ***administration*** in humans, it could be a useful adjunct to boost the efficacy of DC-based vaccines designed against tumours or virus-infected cells.
Title: Enhanced maturation and functional capacity of monocyte-derived immature dendritic cells by the synthetic immunomodulator Murabutide
, 2001
...Abstract: Murabutide on immunophenotype, endocytosis, T-cell stimulatory capacity, and cytokine secretion of human monocyte-derived ***immature*** ***dendritic*** cells (iDCs). We found that Murabutide triggers immunophenotypic changes as upon treatment, iDCs up-regulate ...

...the major histocompatibility complex type II molecule human leucocyte antigen-DR, the co-stimulatory molecules CD80, CD86 and CD40 and the differentiation marker CD83, and down-regulate the expression of the mannose...

...triggers the maturation and activation of monocyte-derived iDCs. As this immunomodulator is approved for administration in humans, it could be a useful adjunct to boost the efficacy of DC-based...
...Identifiers--COLONY-STIMULATING FACTOR; T-CELLS; INFECTED INDIVIDUALS; MURAMYL PEPTIDES; TUMOR VACCINES; HUMAN BLOOD; IN-VIVO; ANTIGEN; ACTIVATION; INTERFERON

13/3,K,AB/3 (Item 2 from file: 34)
DIALOG(R)File 34:SCISEARCH(R) CITED REF SCI

08677321 Genuine Article#: 315VP Number of References: 13
Title: Generation of immature autologous clinical grade dendritic cells for vaccination of cancer patients (ABSTRACT AVAILABLE)
Author(s): Toungouz M (REPRINT) ; Quinet C; Thille E; Fourez S; Pradier O; Delville JP; Velu T; Lambermont M
Corporate Source: FREE UNIV BRUSSELS,HOP ERASME, CELLULAR & MOL THERAPY UNIT, 808 ROUTE LENNIK/B-1070 BRUSSELS//BELGIUM/ (REPRINT); FREE UNIV BRUSSELS,HOP ERASME, DEPT HEMATOL/B-1070 BRUSSELS//BELGIUM/; FREE UNIV BRUSSELS,HOP ERASME, DEPT MED ONCOL/B-1070 BRUSSELS//BELGIUM/
Journal: CYTOTHERAPY, 1999, V1, N6, P447-453
ISSN: 1465-3249 Publication date: 19990000
Publisher: ISIS MEDICAL MEDIA LTD, 59 ST ALDATES, OXFORD OX1 1ST, ENGLAND
Language: English Document Type: ARTICLE
Abstract: Background

Dendritic cell (DC)-based vaccine is a promising approach for ***cancer*** therapy. Pioneer trials have been conducted using DC generated in research conditions. There is now a need for generating DC in clinical grade conditions, including the use of closed systems, avoidance of FCS and respect of good manufacturing practices (GMP).

Methods

DC were generated from 84 leukapheresis products of 27 cancer patients enrolled in two Phase I/II trials of vaccination of either MAGE + ***tumors*** (n = 24) or prostate ***cancer*** (n = 3). Monocytes were seeded in culture bags in a serum-free medium supplemented with IL-4 and GM-CSF. After a 7 day culture, DC were collected and most were pulsed with various MAGE-derived peptides.

Results

After a short leukapheresis (mean time: 66 min; mean processed blood: 5 L), a mean of 6 x 10(9) WBC were collected, from which 2.25% x 10(9) were seeded. The culture procedure yielded a large number of DC (mean: 62 x 10(6) DC) harboring the expected phenotype of immature DC (CD1a(+) CD14(-) HLA-DR+ ***CD80*** (+) ***CD86*** (+) CD83(-)). This phenotype was not altered by peptide loading. These DC, either fresh or thawed, were functionally effective in vitro. Their s.c. and i.v. injections were devoid of any short-term side effect and associated with the induction of immune responses in the patients.

Discussion

Large numbers of functional immature clinical grade DC can be generated in a closed system from leukapheresis products in ***cancer*** patients. These results provide the basis for large-scale studies of cancer immunotherapy under improved safety conditions.

Title: Generation of immature autologous clinical grade dendritic cells for vaccination of cancer patients
, 1999
Abstract: Background

Dendritic cell (DC)-based vaccine is a promising approach for ***cancer*** therapy. Pioneer trials have been conducted using DC generated in research conditions. There is now...

...of good manufacturing practices (GMP).

Methods

DC were generated from 84 leukapheresis products of 27 cancer patients enrolled in two Phase I/II trials of vaccination of either MAGE + ***tumors*** (n = 24) or prostate ***cancer*** (n = 3). Monocytes were seeded in culture bags in a serum-free medium supplemented with...

...x 10(6) DC) harboring the expected phenotype of immature DC (CD1a(+) CD14(-) HLA-DR+ ***CD80*** (+) ***CD86*** (+) CD83(-)). This phenotype was not altered by peptide loading. These DC, either fresh or thawed, were functionally effective in vitro. Their s.c. and i.v. injections were devoid of any short-term side effect and associated with the induction of immune...

...immature clinical grade DC can be generated in a closed system from leukapheresis products in ***cancer*** patients. These results provide the basis for large-scale studies of cancer immunotherapy under improved safety conditions.

?

tle: Vaccination with mouse mammary adenocarcinoma cells coexpressing B7-1 (CD80) and B7-2 (CD86) discloses the dominant effect of B7-1 in the induction of antitumor immunity (ABSTRACT AVAILABLE)
Author(s): MartinFontecha A; Moro M; Crosti MC; Veglia F; Casorati G; Dellabona P (REPRINT)
Corporate Source: SAN RAFFAELE SCI INST,CANC IMMUNOTHERAPY & GENE THERAPY PROGRAM, DIBIT, UNITA IMMUNOCHIM/I-20132 MILAN//ITALY/ (REPRINT); SAN RAFFAELE SCI INST,CANC IMMUNOTHERAPY & GENE THERAPY PROGRAM, DIBIT, UNITA IMMUNOCHIM/I-20132 MILAN//ITALY/; SAN RAFFAELE SCI INST,UNITA BIOSTAT/I-20132 MILAN//ITALY/
Journal: JOURNAL OF IMMUNOLOGY, 2000, V164, N2 (JAN 15), P698-704
ISSN: 0022-1767 Publication date: 20000115
Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814
Language: English Document Type: ARTICLE
Abstract: Nonreplicating TS/A mammary adenocarcinoma cells expressing B7-2 (CD86) (TS/A-2) are more immunogenic than those expressing B7-1 (CD80) (TS/A-1), indicating that B7-1 and B7-2 display nonredundant costimulatory effects in inducing antitumor responses. Whereas transfection of B7-2 cDNA into TS/A-1 cells does not improve their immunogenicity, transfection of B7-1 cDNA into TS/A-2 cells (TS/A-2/1) decreases their immunogenicity in a manner that is directly related to the surface levels of B7-1. Ab blacking of B7-1 on TS/A-2/1 cells before their injection in vivo restores the higher immunogenicity characteristic of single B7-2 transfectants, indicating therefore that B7-1 actively modulates the B7-2-dependent costimulation, The expression of B7-1 also modifies quantitatively the balance of endogenous IFN-gamma and IL-4 induced in vivo by TS/A-2 vaccines. In fact, we find that vaccination with TS/A-2/1 cells results in the production of more IFN-gamma and less IL-4 than TS/A-2 vaccines, a pattern comparable to that induced by TS/A-1 cells. Thus, in the TS/A model of antitumor response, B7-1 modulates B7-2-dependent costimulatory effects in a dominant, noncompetitive way.

Title: Vaccination with mouse mammary adenocarcinoma cells coexpressing B7-1 (CD80) and B7-2 (CD86) discloses the dominant effect of B7-1 in the induction of antitumor immunity
, 2000
Abstract: Nonreplicating TS/A mammary adenocarcinoma cells

Acute Myeloid Leukemia Cells Can Fully Differentiate into Functionally Competent Mature Dendritic Cells That Can Be Used as a Vaccine.

AUTHOR: Cignetti Alessandro (Reprint); Vallario Antonella (Reprint); Roato Ilaria (Reprint); Allione Bernardino (Reprint); Ghia Paolo (Reprint); Caligaris-Cappio Federico (Reprint)
AUTHOR ADDRESS: Laboratory of Tumor Immunology, Institute for Cancer Research and Treatment, Candiolo, TO, Italy**Italy

JOURNAL: Blood 100 (11): pAbstract No. 2166 November 16, 2002 ***2002***
MEDIUM: print
CONFERENCE/MEETING: 44th Annual Meeting of the American Society of Hematology Philadelphia, PA, USA December 06-10, 2002; 20021206
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Acute myeloid leukemia (AML) cells can be induced to differentiate ***in*** ***vitro*** into ***dendritic*** cells (DC). When GM-CSF, TNF-alpha and IL-4 are used as differentiating agents, the leukemia-derived DC display a phenotype of immature DC (iDC), i.e. they express CD80 and CD1a but not CD83, which is a marker of DC maturation. Leukemia specific T cells can be generated in vitro using autologous leukemic DC as antigen presenting cells (APC). Therefore, there is a rationale for using leukemic DC as a tumor vaccine to elicit a T cell response in vivo. It has been shown recently that normal iDC might have an inhibitory effect on T cell function when injected in humans and that mature DC (mDC) are the most potent APC for efficient T cell priming. We aimed at determining whether iDC of leukemic origin can be further differentiated into mature DC (mDC). We analyzed AML cells from 22 patients for their capability to differentiate to iDC and then to reach full maturation to mDC following stimulation with CD40L. Phenotypic criteria for differentiation were set as follows: cultures where gtoreq50% cells expressed CD80 and/or CD1a after stimulation with GM-CSF, TNF-alpha and IL-4 were considered to be iDC, whereas cultures where at least 40% of the CD80+ cells co-expressed CD83 after stimulation with CD40L were considered to be mDC. Following these criteria, iDC were generated in 12/22 cases and they could be induced to fully differentiate into mDC in 8/9 evaluable cases. The following functional parameters were evaluated on leukemic iDC and mDC and compared to those of normal counterparts obtained from both CD34+ and CD14+ precursors: a) Migration in response to constitutive chemokines; b) Attraction of naive and memory T cells; c) Polarization of Th cells; d) Stimulation of allogenic T-cells in mixed lymphocyte-tumor culture (MLTC). e) Generation of autologous effectors in MLTC. We show that: a) leukemic mDC but not iDC express CCR7 and migrate in response to MIP-3beta; b) both iDC and mDC produce MDC and TARC and supernants from DC cultures induce the migration of CCR4+ activated/memory T cells; moreover, mDC but not iDC express mRNA for MIP-3beta and PARC, two chemokines which are normally produced by maturing DC, and supernatants from DC cultures induce the migration of CCR7+ resting/naive T cells; c) leukemic blasts do not express IL-12 and IL-15 and their expression and production are progressively up-regulated along with maturation from blasts to iDC and then to mDC; conversely, leukemic blasts produce and/or express mRNA for IL-10 and this expression is progressively down-regulated along with maturation; d) leukemic mDC have a significantly higher stimulatory activity on T cells than leukemic iDC, similarly to normal DC; e) in one case analyzed, stimulation of patient's lymphocytes with autologous leukemic mDC generated leukemia-specific and MHC-restricted CD4+ T cells. In preliminary experiments, irradiation of leukemic iDC after CD40L stimulation did not affect their differentiation to mDC in terms of phenotype and cytokine production. Taken together, these data indicate that AML cells can be induced to fully differentiate

into functionally competent mDC and lay the ground for testing the efficacy of leukemic mDC as a vaccine aimed at eradicating minimal residual disease in AML patients.

2002

ABSTRACT: Acute myeloid leukemia (AML) cells can be induced to differentiate ***in*** ***vitro*** into ***dendritic*** cells (DC). When GM-CSF, TNF-alpha and IL-4 are used as differentiating agents, the leukemia-derived DC display a phenotype of immature DC (iDC), i.e. they express CD80 and CD1a but not CD83, which is a marker of DC maturation. Leukemia specific T...

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330807 PMID: 9144465

In vivo migration of dendritic cells differentiated in ***vitro*** : a chimpanzee model.

Barratt-Boyes S M; Watkins S C; Finn O J

Department of Molecular Genetics and Biochemistry, School of Medicine, University of Pittsburgh, PA 15261, USA.

Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) May 15 1997, 158 (10) p4543-7, ISSN 0022-1767--Print Journal Code: 2985117R

Contract/Grant Number: 5P30CA47904; CA; NCI; CA557820; CA; NCI; RR00119; RR; NCRR; +

Publishing Model Print

Document type: Journal Article; Research Support, U.S. Gov't, P.H.S.

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Dendritic cells with potent Ag-presenting function can be propagated from peripheral blood using recombinant cytokines, and these cells have potential usefulness as immunotherapeutic agents in the treatment of ***cancer*** and other disease states. However, it is not known if these in vitro differentiated dendritic cells have the capacity to migrate in vivo, especially to T cell areas of lymphoid tissue. We have used a fluorescent marker system to track the migration of dendritic cells, propagated in vitro from chimpanzee peripheral blood, following s.c. ***injection*** . We report that ***injected*** dendritic cells migrate spontaneously and rapidly to draining lymph nodes, where they remain for at least 5 days. The ***injected*** cells interdigitate with T cells in the parafollicular and paracortical zones and retain high level expression of CD86 , CD40, and MHC class II molecules, reflecting a phenotype of potent APC. We conclude that ***dendritic*** cells differentiated in vitro from peripheral blood and ***administered*** s.c. behave in a manner very similar to endogenous Langerhans cells. These data provide strong experimental support, in a highly relevant large animal model, for the use of in vitro differentiated ***dendritic*** cells as vehicles for ***immunotherapy*** . More importantly, they show that the s.c. route of ***injection*** delivers these APC to sites of T cell activation, a prerequisite for the generation of an effective immune response.

Gene immunotherapy in murine acute myeloid leukemia: granulocyte-macrophage colony-stimulating factor tumor cell vaccines elicit more potent antitumor immunity compared with B7 family and other cytokine vaccines.

Dunussi-Joannopoulos K; Dranoff G; Weinstein H J; Ferrara J L; Bierer B E ; Croop J M

Dana-Farber Cancer Institute and Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA.

Blood (UNITED STATES) Jan 1 1998, 91 (1) p222-30, ISSN 0006-4971--Print Journal Code: 7603509

Publishing Model Print

Document type: Comparative Study; Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

In an attempt to explore novel treatment modalities in acute myeloid leukemia (AML), we studied the role of costimulatory and cytokine gene ***immunotherapy*** in murine AML. We have previously shown that leukemic mice can be cured with ***CD80*** transfected leukemic cells (B7. 1-AML vaccine) administered early in the course of the disease and that the failure B7.1-AML vaccines ***administered*** late cannot be attributed to immunosuppression induced by ***tumor*** growth. CD8+ T cells, which are necessary for tumor rejection, are activated rather than suppressed during the first half of the leukemic course in nonvaccinated mice. In this report, we question whether ***CD86*** (B7.2) or the cytokines granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-4 (IL-4), or tumor necrosis factor-alpha (TNF-alpha) can improve the vaccination potential of AML cells. The choice of cytokines was based on their combined and alone as well ability to direct the differentiation of CD34+ cells into potent antigen-presenting dendritic cells in ***vitro*** . Our studies show that (1) mice vaccinated with a leukemogenic number of AML cells engineered to express B7.2 (B7.2-AML) or to secrete GM-CSF, IL-4, or TNF-alpha (GM-, IL-4-, TNF-alpha-AML) do not develop leukemia; (2) GM-AML cells are tumorigenic in sublethally irradiated SJL/J mice but not in Swiss nu/nu mice, indicating that killing of tumor cells is not T-cell-dependent; (3) vaccines with irradiated GM-AML, but not B7.2-, IL-4-, or TNF-alpha-AML cells, can elicit leukemia-specific protective and therapeutic immunity; and (4) in head-to-head comparison experiments, vaccination with irradiated GM-AML is more potent than B7.1-AML, curing 80% and providing 20% prolonged survival of the leukemic mice at week 2, as opposed to cures only up to 1 week with B7.1-AML vaccines. These preclinical data emphasize that GM-CSF gene ***immunotherapy*** deserves clinical evaluation in AML.

Gene immunotherapy in murine acute myeloid leukemia: granulocyte-macrophage colony-stimulating factor tumor cell vaccines elicit more potent antitumor immunity compared with B7 family and other cytokine vaccines.

... ***1998*** ,

... modalities in acute myeloid leukemia (AML), we studied the role of costimulatory and cytokine gene ***immunotherapy*** in murine AML. We have previously shown that leukemic mice can be cured with CD80 transfected leukemic cells (B7. 1-AML vaccine) ***administered*** early in the course of the disease and that the failure B7.1-AML vaccines administered late cannot be attributed to immunosuppression induced by ***tumor*** growth. CD8+ T cells, which are necessary for ***tumor*** rejection, are activated rather than suppressed during the first half of the leukemic course in nonvaccinated mice. In this report, we question whether ***CD86*** (B7.2) or the cytokines granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-4 (IL-4), or tumor necrosis factor-alpha (TNF-alpha) can improve the vaccination potential of AML cells. The choice...

... alone as well ability to direct the differentiation of CD34+ cells into

potent antigen-presenting ***dendritic*** cells ***in*** ***vitro*** . Our
studies show that (1) mice vaccinated with a leukemogenic number of AML
cells engineered...

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tumorigenic in sublethally irradiated SJL/J mice but not in Swiss
nu/nu mice, indicating that killing of tumor cells is not
T-cell-dependent; (3) vaccines with irradiated GM-AML, but not B7...

... 1 week with B7.1-AML vaccines. These preclinical data emphasize that
GM-CSF gene ***immunotherapy*** deserves clinical evaluation in AML.
Descriptors: *Antigens, CD--immunology--IM; *Antigens, CD80
--immunology--IM; *Cancer Vaccines--therapeutic use--TU; *Cytokines
--immunology--IM; *Gene Therapy; *Granulocyte-Macrophage Colony-Stimulating
Factor--immunology--IM; *Immunotherapy, Active; *Leukemia, Myeloid
--therapy--TH; *Leukemia, Radiation-Induced--therapy--TH; *Membrane
Glycoproteins--immunology--IM; *Neoplasm Transplantation; *
Tumor Stem Cells--transplantation--T

11/3,K,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12817624 PMID: 10931381
Characterization of murine dendritic cells derived from adherent blood mononuclear cells in vitro.
Agger R; Petersen M S; Toldbod H E; Holtz S; Dagnaes-Hansen F; Johnsen B W; Bolund L; Hokland M
Department of Medical Microbiology and Immunology, University of Aarhus, Aarhus, Denmark. Agger@microbiology.au.dk
Scandinavian journal of immunology (ENGLAND) Aug 2000, 52 (2) p138-47, ISSN 0300-9475--Print Journal Code: 0323767
Publishing Model Print
Document type: In Vitro; Journal Article; Research Support, Non-U.S. Gov't
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
The therapeutic potential of dendritic cells loaded with tumour antigens for the induction of effective immune responses against cancer is currently being tested in numerous clinical trials. In most cases, the dendritic cells are generated in vitro from peripheral blood monocytes. Many aspects of dendritic cell-based vaccination have not yet been examined in detail, and homologous mouse model systems may prove very valuable for optimizing clinical procedures. In the murine system, however, dendritic cells are usually isolated from either lymphoid tissues or bone marrow cultures. To date, murine monocyte-derived dendritic cells have been described only sporadically. Here, we describe a culture system for the generation of murine dendritic cells from adherent peripheral blood mononuclear cells by culturing in the presence of granulocyte-macrophage colony stimulating factor and interleukin-4. After 7 days of culture the nonadherent cells were harvested from the cultures. Most of these cells exhibited well-accepted characteristics of mature dendritic cells (e.g. veiled appearance, high expression of major histocompatibility complex class II and CD86) and stimulated vigorous proliferation of allogeneic T cells in a primary mixed leucocyte reaction following stimulation with bacterial lipopolysaccharide. Interestingly, staining the cells for expression of the putative antigen-uptake receptor DEC-205 revealed a distinct bimodal distribution.

... ***2000*** ,
... of dendritic cells loaded with tumour antigens for the induction of effective immune responses against cancer is currently being tested in numerous clinical trials. In most cases, the ***dendritic*** cells are generated ***in*** ***vitro*** from peripheral blood monocytes. Many aspects of dendritic cell-based vaccination have not yet been...
... dendritic cells (e.g. veiled appearance, high expression of major histocompatibility complex class II and CD86) and stimulated vigorous proliferation of allogeneic T cells in a primary mixed leucocyte reaction following...
; Animals; Antigens, Neoplasm--administration and dosage--AD; Cancer Vaccines--administration and dosage--AD; Cell Adhesion; Cell Culture Techniques--methods--MT; Cell Differentiation; Cell Separation ; Dendritic...

...CY; Leukocytes, Mononuclear--immunology--IM; Lymphocyte Activation; Lymphocyte Culture Test, Mixed; Mice; Mice, Inbred C57BL; Neoplasms --immunology--IM; Neoplasms--therapy--TH; Phenotype; T-Lymphocytes --immunology--IM
Chemical Name: Antigens, Neoplasm; Cancer Vaccines

11/3,K,AB/4 (Item 4 from file: 155)

11664340 PMID: 9414288

Gene immunotherapy in murine acute myeloid leukemia: granulocyte-macrophage colony-stimulating factor tumor cell vaccines elicit more potent antitumor immunity compared with B7 family and other cytokine vaccines.

Dunussi-Joannopoulos K

Intratumoral injection of dendritic cells derived in ***vitro*** in patients with metastatic ***cancer*** .

Triozzi P L; Khurram R; Aldrich W A; Walker M J; Kim J A; Jaynes S
The Arthur G. James Cancer Hospital and Richard J. Solove Research Institute/The Ohio State University Comprehensive Cancer Center, Columbus, Ohio, USA. pierre.triozzi@ccc.uab.edu

Cancer (UNITED STATES) Dec 15 2000, 89 (12) p2646-54, ISSN 0008-543X--Print Journal Code: 0374236
Contract/Grant Number: P30CA16058; CA; NCI; R01 CA67830-01; CA; NCI
Publishing Model Print
Document type: Clinical Trial; Controlled Clinical Trial; Journal Article ; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

BACKGROUND: Dendritic cells (DCs) are potent initiators of immune responses, and the infiltration of DCs into tumors may confer an improved prognosis. Whether the ***injection*** of DCs directly into ***tumors*** can mediate biologic activity was examined. METHODS: Patients with metastatic dermal or subcutaneous tumors received granulocyte-macrophage-colony stimulating factor to increase the numbers of peripheral blood monocyte precursors. DCs were then generated from monocytes obtained by phlebotomy with granulocyte-macrophage-colony stimulating factor and interleukin-4 in autologous plasma. ***Tumors*** were injected at multiple sites with 30 million autologous DCs per ***tumor*** . RESULTS: Seven patients with melanoma and three patients with breast carcinoma were treated. ***Injections*** were well tolerated. Regression of the injected tumors, beginning as early as 4 days after injection , was observed in four patients with melanoma and in two patients with breast carcinoma. Biopsies of regressing lesions showed lymphocyte infiltration associated with DCs and necrosis. Neutrophils and macrophages were not evident. Lymphocytes expanded from the regressing tumors proliferated in response to heat shock proteins, HSP70 and gp96, derived from autologous ***tumor*** . The DCs ***injected*** produced interferon-alpha and expressed Fas ligand mRNA but did not exhibit cytolytic activity in vitro. Expression of the costimulatory molecule, B7-2 (***CD86***), decreased on DCs after intratumoral ***injection*** . CONCLUSIONS: This pilot study demonstrates that DCs derived in vitro can exist viably after intratumoral injection and can mediate biologic activity in situ. ***Tumor*** -derived heat shock proteins may be involved in the antitumor activity observed. Copyright 2000 American ***Cancer*** Society.

Intratumoral injection of dendritic cells derived in ***vitro*** in patients with metastatic ***cancer*** .

... ***2000*** ,

... Dendritic cells (DCs) are potent initiators of immune responses, and the infiltration of DCs into ***tumors*** may confer an improved prognosis. Whether the injection of DCs directly into tumors can mediate biologic activity was examined. METHODS: Patients with metastatic dermal or subcutaneous tumors received granulocyte-macrophage-colony stimulating factor to increase the numbers of peripheral blood monocyte precursors...

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Descriptors: *Dendritic Cells--immunology--IM; *Immunotherapy , Adoptive; *Neoplasms--therapy--TH; Adult; Aged; Antigens, CD --analysis--AN; Antigens, CD86; Cell Transplantation; Dendritic Cells --transplantation--TR; Flow Cytometry; HLA-DR Antigens--analysis--AN; Heat-Shock Proteins--analysis--AN; Humans; Immunohistochemistry; Injections, Intralesional; Integrin alphaXbeta2--analysis--AN; Membrane Glycoproteins--analysis--AN; Middle Aged; Neoplasm

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YSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R) 1950-2007/Sep 28
        (c) format only 2007 Dialog
  File  55:Biosis Previews(R) 1993-2007/Sep W5
        (c) 2007 The Thomson Corporation
  File  34:SCISEARCH(R) CITED REF SCI 1990-2007/SEP W4
        (c) 2007 THE THOMSON CORP
  File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
        (c) 2006 The Thomson Corp
  File 340:CLAIMS(R)/US Patent 1950-07/Sep 27
        (c) 2007 IFI/CLAIMS(R)
*File 340: The 2006 reload is online as of December 1, 2006.
IPCR/8 is available.

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        40012489  IN
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         1623718  IN(W)VITRO
          161944  DENDRITIC
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         2694423  ADMINIST?
      S2 3628147  INJECT? OR ADMINIST?
? s s1 and s2
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         2378413  NEOPLAS?
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         4530706  S4
      S5     534  S3 AND S4
? s pulsed
      S6  181530  PULSED
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             534  S5
          181530  S6
      S7     417  S5 NOT S6
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>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
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           11981  CD86
            6575  CD54
     S10   21460  CD80 OR CD86 OR CD54
? s s9 and s10
             103  S9
           21460  S10
     S11      11  S9 AND S10
? t s11/3,k,ab/1-11

 11/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2007 Dialog. All rts. reserv.
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14020155 PMID: 12393401

Stressed apoptotic tumor cells stimulate dendritic cells and induce specific cytotoxic T cells.

Feng Hanping; Zeng Yi; Graner Michael W; Katsanis Emmanuel

Department of Pediatrics, Steele Memorial Children's Research Center, University of Arizona, Tucson 85724, USA.

Blood (United States) Dec 1 2002, 100 (12) p4108-15, ISSN 0006-4971--Print Journal Code: 7603509

Publishing Model Print-Electronic

Document type: Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

We have previously reported that stressed apoptotic tumor cells are more immunogenic in vivo than nonstressed ones. Using confocal microscopy we have confirmed our previous observation that heat-stressed apoptotic 12B1-D1 leukemia cells (BCR-ABL(+)) express HSP60 and HSP72 on their surface. To explore how the immune system distinguishes stressed from nonstressed apoptotic tumor cells, we analyzed the responses of dendritic cells to these 2 types of apoptotic cells. We found that nonstressed and heat-stressed apoptotic 12B1-D1 cells were taken up by dendritic cells in a comparable fashion. However, when stressed apoptotic 12B1-D1 cells were coincubated with immature dendritic cells for 24 hours, this resulted in greater up-regulation of costimulatory molecules (CD40, CD80, and CD86) on the surface of dendritic cells. Moreover, stressed apoptotic 12B1-D1 cells were more effective in stimulating dendritic cells to secrete interleukin-12 (IL-12) and in enhancing their immunostimulatory functions in mixed leukocyte reactions. Furthermore, we demonstrated that immunization of mice with stressed apoptotic 12B1-D1 cells induced the secretion of T helper-1 (T(H)1) profile of cytokines by spleen cells. Splenocytes from mice immunized with stressed apoptotic cells, but not nonstressed ones, were capable of lysing 12B1-D1 and the parental 12B1 line, but not a B-cell leukemia line, A20. Our data indicate that stressed apoptotic tumor cells are capable of providing the necessary danger signals, likely through increased surface expression of heat shock proteins (HSPs), resulting in activation/maturation of dendritic cells and, ultimately, the generation of potent antitumor T-cell responses.

Stressed apoptotic tumor cells stimulate dendritic cells and induce specific cytotoxic T cells.

... ***2002*** ,

We have previously reported that stressed apoptotic tumor cells are more immunogenic in vivo than nonstressed ones. Using confocal microscopy we have confirmed...

... HSP72 on their surface. To explore how the immune system distinguishes stressed from nonstressed apoptotic tumor cells, we analyzed the responses of dendritic cells to these 2 types of apoptotic cells...

... cells in a comparable fashion. However, when stressed apoptotic 12B1-D1 cells were coincubated with immature dendritic cells for 24 hours, this resulted in greater up-regulation of costimulatory molecules (CD40, ***CD80*** , and ***CD86***) on the surface of dendritic cells. Moreover, stressed apoptotic 12B1-D1 cells were more effective...

... line, but not a B-cell leukemia line, A20. Our data indicate that stressed apoptotic tumor cells are capable of providing the necessary danger signals, likely through increased surface expression of...
; Animals; Bone Marrow Cells; Cancer Vaccines--administration and dosage--AD; Cancer Vaccines--pharmacology--PD; Chaperonin 60 --metabolism--ME; HSP72 Heat-Shock Proteins; Heat-Shock Proteins --metabolism...

...pathology--PA; Lymphocyte Activation--immunology--IM; Lymphocyte Culture Test, Mixed; Mice; Mice, Inbred BALB C; Tumor Cells, Cultured
Chemical Name: Cancer Vaccines; Chaperonin 60; HSP72 Heat-Shock Proteins; Heat-Shock Proteins

11/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11211193 PMID: 8985101

Bacillus Calmette-Guerin mycobacteria stimulate human blood ***dendritic*** cells.

Thurnher M; Ramoner R; Gastl G; Radmayr C; Bock G; Herold M; Klocker H; Bartsch G

Department of Urology, University of Innsbruck, Austria.

International journal of cancer. Journal international du cancer (UNITED STATES) Jan 6 1997, 70 (1) p128-34, ISSN 0020-7136--Print
Journal Code: 0042124

Publishing Model Print

Document type: Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Bacillus Calmette-Guerin (BCG) mycobacteria have been used as adjuvant in the active immunotherapy of various human cancers. In addition, dendritic cells, which are the most potent antigen-presenting cells, have been shown to be capable of initiating anti-tumor immune responses. Here we investigated the effects of BCG on dendritic cells cultured from human blood. Addition of ***BCG*** resulted in rapid homotypic adhesion of ***dendritic*** cells. Moreover, ***BCG*** concentrations ranging from 10(4) to 10(6) bacteria/ml enhanced expression of the dendritic-cell-maturation antigen CD83 and of the T-cell co-stimulator ***CD86*** (B7-2) in a dose-dependent manner. Concomitant with the increase of CD83 and CD86 expression, the cells lost the ability to capture soluble antigens, as determined by the exclusion of fluoresceinated Dextran molecules. Strikingly, the same dosages of BCG -bacteria stimulated TNF-alpha-gene transcription and TNF-alpha-protein release from dendritic cells in a dose-dependent fashion. ***BCG*** infection of ***dendritic*** cells in the presence of a neutralizing antibody directed against TNF-alpha inhibited CD83 expression by more than 50% indicating that the BCG-induced maturation of dendritic cells was at least partially mediated by dendritic -cell-derived TNF-alpha. The finding that ***BCG*** activates the most potent antigen-presenting cells reveals a plausible immunological mechanism of the occasionally observed anti-tumor activity of ***BCG*** .

Protection against aerosol Mycobacterium tuberculosis infection using Mycobacterium bovis Bacillus Calmette Guerin-infected dendritic cells.

Demangel C; Bean A G; Martin E; Feng C G; Kamath A T; Britton W J
Centenary Institute of Cancer Medicine and Cell Biology, Newtown, NSW, Australia.

European journal of immunology (GERMANY) Jun 1999, 29 (6) p1972-9, ISSN 0014-2980--Print Journal Code: 1273201
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

In the lung, dendritic cells (DC) are key antigen-presenting cells capable of triggering specific cellular responses to inhaled pathogens, and thus, they may be important in the initiation of an early response to mycobacterial infections. The ability of DC to enhance antigen presentation to naive T cells within the lungs was characterized with respect to Mycobacterium bovis Bacillus Calmette Guerin (BCG) vaccination against M. tuberculosis infection. In vitro derived DC were infected with BCG, which induced their maturation, as shown by the increased expression of MHC class II antigens, CD80 and CD86 co-stimulatory molecules. The synthesis of mRNA for IL-1, IL-6, IL-12, IL-10 and IL-1 receptor antagonist was also enhanced. When administered intratracheally in mice, infected DC induced a potent T cell response and the production of IFN-gamma to mycobacterial antigens in the mediastinal lymph nodes, leading to a significant protection against aerosol M. tuberculosis infection. Intriguingly, although the vaccination schedule for BCG-infected DC was much shorter than subcutaneous BCG vaccination (7 days as compared to 100 days), both types of vaccination showed similar levels of protection. These data confirm that DC can be potent inducers of a cellular immune response against mycobacteria and support the concept of combining DC strategies with mycobacterial vaccines for protective immunity against tuberculosis.

Maturation of human dendritic cells by cell wall skeleton of Mycobacterium bovis bacillus Calmette-Guerin: involvement of toll-like receptors.

Tsuji S; Matsumoto M; Takeuchi O; Akira S; Azuma I; Hayashi A; Toyoshima K; Seya T

Department of Immunology, Osaka Medical Center for Cancer and Cardiovascular Diseases, Higashinari-ku, Osaka 537-8511, Japan.

Infection and immunity (UNITED STATES) Dec 2000, 68 (12) p6883-90, ISSN 0019-9567--Print Journal Code: 0246127

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

The constituents of mycobacteria are an effective immune adjuvant, as observed with complete Freund's adjuvant. In this study, we demonstrated that the cell wall skeleton of Mycobacterium bovis bacillus Calmette-Guerin (BCG -CWS), a purified noninfectious material consisting of peptidoglycan, arabinogalactan, and mycolic acids, induces maturation of human ***dendritic*** cells (DC). Surface expression of CD40, CD80, CD83, and CD86 was increased by BCG-CWS on human immature DC, and the effect was similar to those of interleukin-1beta (IL-1beta), tumor necrosis factor alpha (TNF-alpha), heat-killed BCG, and viable ***BCG*** . ***BCG*** -CWS induced the secretion of TNF-alpha, IL-6, and IL-12 p40. CD83 expression was increased by a soluble factor secreted from BCG -CWS-treated DC and was completely inhibited by monoclonal antibodies against TNF-alpha. ***BCG*** -CWS-treated DC stimulated extensive allogeneic mixed lymphocyte reactions. The level of TNF-alpha secreted through BCG -CWS was partially suppressed in murine macrophages with no Toll-like receptor 2 (TLR 2) or TLR4 and was completely lost in TLR2 and TLR4 double-deficient macrophages. These results suggest that the ***BCG*** -CWS induces TNF-alpha secretion from DC via TLR2 and TLR4 and that the secreted TNF-alpha induces the ***maturation*** of DC per se.

```
      ---  -----  -----------
? s bcg
      S1   38298  BCG
? s dendritic
      S2  161970  DENDRITIC
? s s1 and s2
           38298  S1
          161970  S2
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? rd

>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
      S6      78  RD  (unique items)
? s s6 and py<2002
Processing
Processing
              78  S6
        42339596  PY<2002
      S7      18  S6 AND PY<2002
? s cd86
      S8   11985  CD86
? s s7 and s8
              18  S7
           11985  S8
      S9       6  S7 AND S8
? t s9/3,k,ab/1-6

 9/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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12944641   PMID: 11083809
   Maturation of human dendritic cells by cell wall skeleton of
Mycobacterium bovis bacillus Calmette-Guerin: involvement of toll-like
receptors.
  Tsuji S; Matsumoto M; Takeuchi O; Akira S; Azuma I; Hayashi A; Toyoshima
K; Seya T
  Department of Immunology, Osaka Medical Center for Cancer and
Cardiovascular Diseases, Higashinari-ku, Osaka 537-8511, Japan.
  Infection and immunity (UNITED STATES) Dec 2000, 68 (12)
 p6883-90, ISSN 0019-9567--Print Journal Code: 0246127
  Publishing Model Print
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed
  The constituents of mycobacteria are an effective immune adjuvant, as
observed with complete Freund's adjuvant. In this study, we demonstrated
that the cell wall skeleton of Mycobacterium bovis bacillus Calmette-Guerin
(BCG -CWS), a purified noninfectious material consisting of
peptidoglycan, arabinogalactan, and mycolic acids, induces maturation
 of human ***dendritic*** cells (DC). Surface expression of CD40, CD80,
CD83, and CD86 was increased by BCG-CWS on human immature DC,
and the effect was similar to those of interleukin-1beta (IL-1beta), tumor
necrosis factor alpha (TNF-alpha), heat-killed BCG, and viable
  ***BCG*** . ***BCG*** -CWS induced the secretion of TNF-alpha, IL-6, and
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IL-12 p40. CD83 expression was increased by a soluble factor secreted from BCG -CWS-treated DC and was completely inhibited by monoclonal antibodies against TNF-alpha. ***BCG*** -CWS-treated DC stimulated extensive allogeneic mixed lymphocyte reactions. The level of TNF-alpha secreted through BCG -CWS was partially suppressed in murine macrophages with no Toll-like receptor 2 (TLR 2) or TLR4 and was completely lost in TLR2 and TLR4 double-deficient macrophages. These results suggest that the ***BCG***